

**UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS**

DANA-FARBER CANCER INSTITUTE,
INC.,

Plaintiff,

v.

ONO PHARMACEUTICAL CO., LTD.,
TASUKU HONJO, E. R. SQUIBB & SONS,
L.L.C., AND BRISTOL-MYERS SQUIBB,
CO.,

Defendants.

Civil Action No. 1:15-cv-13443-MLW

**DEFENDANTS E. R. SQUIBB & SONS, L.L.C. AND BRISTOL-MYERS SQUIBB, CO.'S
ANSWER**

E. R. Squibb & Sons, L.L.C. and Bristol-Myers Squibb, Co. (collectively, “BMS”), by and through their undersigned counsel, hereby answer the Complaint for correction of inventorship of Dana-Farber Cancer Institute (“Dana-Farber” or “Plaintiff”), in accordance with the numbered paragraphs thereof, as follows. All allegations of fact and conclusions of law contained in the Complaint are denied, except those specifically admitted herein:

Introduction

1. BMS admits that Dana-Farber purports to have brought an action under 35 U.S.C. § 256 seeking to modify the inventorship of U.S. Patent Nos. 7,595,048 (“the ’048 patent”); 8,168,179 (“the ’179 patent”); 8,728,474 (“the ’474 patent”); 9,067,999 (“the ’999 patent”); and 9,073,994 (“the ’994 patent”) (collectively, the “Patents”). BMS admits that what purport to be copies of the Patents are attached as Exhibits A through E. BMS denies that Yoshiko Iwai is currently and that Shiro Shibayama is or was a colleague of Dr. Tasuku Honjo (“Honjo”) at Kyoto University. BMS admits the remaining allegations in this paragraph.

2. BMS admits the Patents claim a pioneering treatment for cancer using cancer immunotherapy. BMS admits that cancer immunotherapy is a way to unleash the body's disease-fighting cells, which include the immune system's T lymphocytes, or "T cells," to make a sustained attack on cancer cells. BMS admits that T cells are a critical component of the body's immune system, recognizing and protecting against viruses and other foreign invaders and also helping to destroy cancer cells. BMS denies the remaining allegations in Paragraph 2 of the Complaint.

3. BMS admits that T cells may express a protein called PD-1 on their surface, and that PD-1 serves as an immune system checkpoint. BMS admits that PD-L1 is a ligand for PD-1. BMS admits that when PD-L1 on a normal cell binds to PD-1 on a T cell, the effect is to inhibit (or "downregulate") the proliferation of T cells, as well as the T cells' expression of certain immune proteins called cytokines. BMS lacks sufficient knowledge or information to form a belief as to the remaining allegations in Paragraph 3 of the Complaint, and therefore denies those allegations.

4. BMS admits that PD-1 was discovered early in the 1990s. BMS admits that PD-L2 is a second ligand for PD-1. BMS lacks sufficient knowledge or information to form a belief as to the remaining allegations in Paragraph 4 of the Complaint, and therefore denies those allegations.

5. BMS admits that PD-L1 is expressed on certain cancer cells and that PD-L1 can interact with PD-1 on T cells to suppress an immune response against cancer cells, which allows them to live on and multiply while escaping attack from the body's T cells. BMS lacks sufficient knowledge or information to form a belief as to the remaining allegations in Paragraph 5 of the Complaint, and therefore denies those allegations.

6. BMS admits that cancer immunotherapy, including the use of antibodies that block the PD-1 checkpoint pathway, allows a patient's immune system to resume its ability to recognize, attack, and destroy cancer cells. BMS denies the remaining allegations in Paragraph 6 of the Complaint.

7. BMS lacks sufficient knowledge or information to form a belief as to Plaintiff's use of a "biological lock and key" analogy, and therefore denies the allegations in Paragraph 7 of the Complaint.

8. BMS admits that in 2014 Honjo and Freeman were two of four recipients of the Cancer Research Institute's William B. Coley Award. BMS lacks sufficient knowledge or information to form a belief as to the remaining allegations in Paragraph 8 of the Complaint, and therefore denies those allegations.

9. BMS admits the Patents issued from 2009 to 2015 and contain claims directed to treating cancer with anti-PD-1 antibodies. BMS admits the Patents list Tasuku Honjo, Nagahiro Minato, Yoshiko Iwai, and Shiro Shibayama as the inventors of the claimed subject matter. BMS denies that Shiro Shibayama is or was and Yoshiko Iwai is currently Honjo's colleague at Kyoto University. BMS lacks sufficient knowledge or information to form a belief as to the remaining allegations in Paragraph 9 of the Complaint, and therefore denies those allegations.

10. BMS admits that its anti-PD-1 antibody, Opdivo[®], and Merck's anti-PD-1 antibody, Keytruda[®], were approved by the FDA in 2014 for the treatment of advanced melanoma. BMS lacks sufficient knowledge or information to form a belief as to the remaining allegations in Paragraph 10 of the Complaint, and therefore denies those allegations.

The Parties

11. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 11 of the Complaint, and therefore denies those allegations.

12. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 12 of the Complaint, and therefore denies those allegations.

13. BMS admits the allegations in Paragraph 13 of the Complaint.

14. BMS admits the allegations in Paragraph 14 of the Complaint.

15. BMS admits that it has an exclusive license to the Patents from Ono, but denies that it has an exclusive license with Honjo. BMS denies that Ono and Honjo exclusively licensed their rights under the Patents to Squibb. BMS admits the remaining allegations in Paragraph 15 of the Complaint.

16. BMS admits the allegations in Paragraph 16 of the Complaint.

17. BMS admits the allegations in Paragraph 17 of the Complaint.

Jurisdiction

18. BMS admits that the Complaint contends that subject-matter jurisdiction exists over this action pursuant to 28 U.S.C. §§ 1331, 1338(a), and 35 U.S.C. § 256.

19. BMS denies the allegations in Paragraph 19 of the Complaint.

20. BMS states that it will not contest that personal jurisdiction exists over BMS and Honjo in the District Court of Massachusetts. BMS denies the District Court of Massachusetts has personal jurisdiction over Ono.

The Freeman/Wood/Honjo Collaboration

21. BMS lacks sufficient knowledge or information to form a belief as to whether Freeman was investigating the “B7” family of proteins in the 1990s, and therefore denies that allegation. BMS admits the remaining allegations in Paragraph 21 of the Complaint.

22. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 22 of the Complaint, and therefore denies those allegations.

23. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 23 of the Complaint, and therefore denies those allegations.

24. BMS admits that PD-1 had been known since the early 1990s. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 24 of the Complaint, and therefore denies those allegations.

25. BMS admits that PD-L1 is a ligand for PD-1. BMS lacks sufficient knowledge or information to form a belief as to the remaining allegations in Paragraph 25 of the Complaint, and therefore denies those allegations.

26. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 26 of the Complaint, and therefore denies those allegations.

27. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 27 of the Complaint, and therefore denies those allegations.

28. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 28 of the Complaint, and therefore denies those allegations.

29. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 29 of the Complaint, and therefore denies those allegations.

30. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 30 of the Complaint, and therefore denies those allegations.

31. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 31 of the Complaint, and therefore denies those allegations.

32. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 32 of the Complaint, and therefore denies those allegations.

33. BMS admits that Honjo, Wood and Freeman are co-authors on the research paper “Engagement of the PD-1 Immunoinhibitory Receptor by a Novel B7 Family Member Leads to Negative Regulation of Lymphocyte Activation,” J. Exp. Med., October 2, 2000. BMS lacks sufficient knowledge or information to form a belief as to the remaining allegations in Paragraph 33 of the Complaint, and therefore denies those allegations.

34. BMS admits the research paper contains five figures reporting experimental data. BMS lacks sufficient knowledge or information to form a belief as to the remaining allegations in Paragraph 34 of the Complaint, and therefore denies those allegations.

35. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 35 of the Complaint, and therefore denies those allegations.

36. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 36 of the Complaint, and therefore denies those allegations.

37. BMS admits that Honjo, Wood and Freeman are co-authors on the research paper “PD-L2 is a second ligand for PD-1 and inhibits T cell activation,” Nature Immunology, March 2001. BMS lacks sufficient knowledge or information to form a belief as to the remaining allegations in Paragraph 37 of the Complaint, and therefore denies those allegations.

The Patents

38. BMS denies that Shiro Shibayama is or was Honjo's colleague at Kyoto University. BMS admits the remaining allegations in Paragraph 38 of the Complaint.

39. BMS denies that Shiro Shibayama is or was Honjo's colleague at Kyoto University. BMS admits the remaining allegations in Paragraph 39 of the Complaint.

40. BMS admits that Claim 1 of the '048 patent is directed to: "A method for treatment of cancer, wherein a pharmaceutically effective amount of completely human anti-PD-1 antibody is parenterally administered to a subject with cancer in which PD-L1 or PD-L2 is over-expressed, postoperatively." BMS denies the remaining allegations in Paragraph 40 of the Complaint.

41. BMS denies that Shiro Shibayama is or was Honjo's colleague at Kyoto University. BMS admits the remaining allegations in Paragraph 41 of the Complaint.

42. BMS admits that Claim 1 of the '179 patent is directed to: "A method of treating a PD-L1-expressing tumor, comprising administering a pharmaceutically effective amount of an anti-PD-L1 antibody to a patient in need thereof, in combination with a pharmaceutically effective amount of one or more chemotherapy drugs, wherein said one or more chemotherapy drugs are selected from the group consisting of an alkylating agent, a nitrosourea agent, an antimetabolite, an antitumor antibiotic, an alkaloid derived from a plant, a topoisomerase inhibitor, a hormone therapy medicine, a hormone antagonist, an aromatase inhibitor, a P-glycoprotein inhibitor and a platinum complex derivative." BMS denies the remaining allegations in Paragraph 42 of the Complaint.

43. BMS denies that Shiro Shibayama is or was Honjo's colleague at Kyoto University. BMS admits the remaining allegations in Paragraph 43 of the Complaint.

44. BMS admits that Claim 1 of the '474 patent is directed to: "A method for treatment of a tumor in a patient, comprising administering to the patient a pharmaceutically effective amount of an anti-PD-1 monoclonal antibody." BMS denies the remaining allegations in Paragraph 44 of the Complaint.

45. BMS denies that Shiro Shibayama is or was Honjo's colleague at Kyoto University. BMS admits the remaining allegations in Paragraph 45 of the Complaint.

46. BMS admits that Claim 1 of the '999 patent is directed to: "A method of treating a lung cancer comprising administering a composition comprising a human or humanized anti-PD-1 monoclonal antibody to a human with the lung cancer, wherein the administration of the composition treats the lung cancer in the human." BMS admits that Claim 19 of the '999 patent is directed to: "The method of claim 1, wherein the lung cancer expresses PD-L1." BMS denies the remaining allegations in Paragraph 46 of the Complaint.

47. BMS denies that Shiro Shibayama is or was Honjo's colleague at Kyoto University. BMS admits the remaining allegations in Paragraph 47 of the Complaint.

48. BMS admits that Claim 1 of the '994 patent is directed to: "A method of treating a metastatic melanoma comprising intravenously administering an effective amount of a composition comprising a human or humanized anti-PD-1 monoclonal antibody and a solubilizer in solution to a human with the metastatic melanoma, wherein the administration of the composition treats the metastatic melanoma in the human." BMS admits that Claim 14 of the '994 patent is directed to: "The method of claim 1, wherein the metastatic melanoma expresses PD-L1." BMS denies the remaining allegations in Paragraph 48 of the Complaint.

49. BMS admits the Patents disclose experiments by Honjo and colleagues using antibodies that block PD-1 or PD-L1 to inhibit the function of the PD-1/PD-L1 pathway and

thereby suppress tumor proliferation. BMS lacks sufficient knowledge or information to form a belief as to the remaining allegations in Paragraph 49 of the Complaint, and therefore denies those allegations.

50. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 50 of the Complaint, and therefore denies those allegations.

51. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 51 of the Complaint, and therefore denies those allegations.

52. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 52 of the Complaint, and therefore denies those allegations.

53. Paragraph 53 of the Complaint contains conclusions of law to which no response is required. To the extent that a response is deemed required, BMS denies the allegations in Paragraph 53 of the Complaint.

54. Paragraph 54 of the Complaint contains conclusions of law to which no response is required. To the extent that a response is deemed required, BMS denies the allegations in Paragraph 54 of the Complaint.

55. BMS denies the allegations of Paragraph 55 of the Complaint.

56. BMS admits that Dana-Farber purportedly seeks an order correcting inventorship of the Patents, but denies that such an order should issue. BMS lacks sufficient knowledge or information to form a belief as to the remaining allegations in Paragraph 56 of the Complaint, and therefore denies those allegations.

Count I
(Correction of Inventorship of United States Patent No. 7,595,048)

57. BMS restates and incorporates by reference its answers to the allegations contained in Paragraphs 1 – 56 as set forth fully herein.

58. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 58 of the Complaint, and therefore denies those allegations.

59. Paragraph 59 of the Complaint contains conclusions of law to which no response is required. To the extent that a response is deemed required, BMS denies the allegations in Paragraph 59 of the Complaint.

Count II
(Correction of Inventorship of United States Patent No. 8,168,179)

60. BMS restates and incorporates by reference its answers to the allegations contained in paragraphs 1 – 59 of the Complaint as set forth fully herein.

61. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 61 of the Complaint, and therefore denies those allegations.

62. Paragraph 62 of the Complaint contains conclusions of law to which no response is required. To the extent that a response is deemed required, BMS denies the allegations in Paragraph 62 of the Complaint.

Count III
(Correction of Inventorship of United States Patent No. 8,728,474)

63. BMS restates and incorporates by reference its answers to the allegations contained in paragraphs 1 – 62 of the Complaint as set forth fully herein.

64. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 64 of the Complaint, and therefore denies those allegations.

65. Paragraph 65 of the Complaint contains conclusions of law to which no response is required. To the extent that a response is deemed required, BMS denies the allegations in Paragraph 65 of the Complaint.

Count IV
(Correction of Inventorship of United States Patent No. 9,067,999)

66. BMS restates and incorporates by reference its answers to the allegations contained in Paragraphs 1 – 65 of the Complaint as if set forth fully herein.

67. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 67 of the Complaint, and therefore denies those allegations.

68. Paragraph 68 of the Complaint contains conclusions of law to which no response is required. To the extent that a response is deemed required, BMS denies the allegations in Paragraph 68 of the Complaint.

Count V
(Correction of Inventorship of United States Patent No. 9,073,994)

69. BMS restates and incorporates by reference its answers to the allegations contained in Paragraphs 1 – 68 of the Complaint as if set forth fully herein.

70. BMS lacks sufficient knowledge or information to form a belief as to the allegations in Paragraph 70 of the Complaint, and therefore denies those allegations.

71. Paragraph 71 of the Complaint contains conclusions of law to which no response is required. To the extent that a response is deemed required, BMS denies the allegations in Paragraph 71 of the Complaint.

PRAYER FOR RELIEF

BMS denies that Dana-Farber is entitled to any relief.

AFFIRMATIVE DEFENSES

BMS asserts the following affirmative defenses in opposition to the cause of action and allegations of the Complaint. BMS reserves the right to add additional affirmative defenses as they are learned through discovery and further investigation.

First Defense
(Failure to State a Claim)

72. The Complaint fails to state a claim upon which relief can be granted.

Second Defense
(Inventorship is Proper)

73. The Patents are presumed valid and, with that, the named inventors of the Patents are presumed correct. Freeman and Wood did not invent or contribute to the conception of the inventions contained in the Patents.

Third Defense
(Laches, Acquiescence, Waiver)

74. Plaintiff is not entitled to relief because of laches, acquiescence, waiver, and/or other applicable doctrines.

Fourth Defense
(Exceptional Case)

75. This case is exceptional under 35 U.S.C. § 285. BMS is entitled to an award of its attorneys' fees and costs incurred in connection with defending and prosecuting this action.

Fifth Defense
(Failure to Join an Indispensable Party)

76. Ono Pharmaceutical Co., Ltd. is a co-owner of the patents at issue and an indispensable party in this case. The Complaint states no basis for jurisdiction, and this Court does not have jurisdiction over Ono Pharmaceutical Co., Ltd. The Complaint must be dismissed for failure to join an indispensable party.

Additional Affirmative Defenses

77. BMS reserves the right to assert additional defenses as they become known through further investigation and discovery.

PRAYER FOR RELIEF

WHEREFORE, BMS prays for relief as follows:

- A. Dismissing the Complaint with prejudice, and denying all relief sought in the Complaint;
- B. Judgment in its favor for all claims for relief;
- C. A declaration that this case is exceptional pursuant to 35 U.S.C. § 285, and an award of attorneys' fees and costs; and
- D. For an award of such other and further relief as the Court may deem just and proper.

Respectfully submitted,

Dated: December 21, 2015

/s/ Kelli J. Powell

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*Counsel for Tasuku Honjo, E. R. Squibb &
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CERTIFICATE OF SERVICE

I hereby certify that a true copy of the above document, filed through the ECF system, will be sent electronically to the registered participants of record as identified on the Notice of Electronic Filing on December 21, 2015.

/s/ Kelli J. Powell

Kelli J. Powell (BBO #682079)